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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,181	09/15/2003	Steven Z. Wu	50623.334	1431

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EXAMINER	
WORSHAM, JESSICA N	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
05/10/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,181	WU ET AL.	
	Examiner	Art Unit	
	JESSICA WORSHAM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,30-32 and 34-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,30-32 and 34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/15/10 and 2/17/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Information Disclosure Statement

1. The information disclosure statements (IDS) submitted on March 15, 2010 and February 17, 2011 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner. See attached copy of PTO-1449.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 15, 2010 has been entered. The application has been transferred to the new examiner of record.

Claims 25, 30-32, and 34-43 are pending in this application. Claims 35-43 are newly added claims but do not add new matter. Claims 1-24, 26-29, and 33 were previously cancelled. Claims 25, 30-32, and 34-43 are examined on the merits herein.

Election/Restriction

4. Applicant's election without traverse of species (c), an ethylene-vinyl alcohol copolymer in the reply filed February 1, 2011 is acknowledged.

New Rejections

Claim Rejections -35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 25, 30-32, 34-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al. in view of Hossainy et al. (hereinafter "Hossainy") (U.S. Patent Application Publication No. 2001/0014717 A1).

The teachings of Hunter et al. are described below in the previous rejections filed on March 27, 2009.

Hunter et al. do not teach a method of coating wherein the polymeric material dissolved in solvent is ethylene-vinyl alcohol copolymer.

Hossainy ('717) teaches a coating composition wherein sufficient amounts of active ingredient are dispersed in a blended composition of ethylene-vinyl alcohol copolymer and solvent. The active ingredient is saturated in the blended composition (i.e. suspended). See page 3, paragraph [0042] and page 6, paragraph [0055]. Claim 1 states a method of forming a coating on an implantable device, comprising forming a primer layer followed by forming a reservoir region containing the active ingredient (or multiple active ingredients). The primer layer provides an adhesive tie between the reservoir coating and the device, allowing for more active agent to be added, since active ingredients in a polymeric matrix interfere with the ability of the

matrix to adhere effectively directly to the surface of the device. See page 4, paragraph [0047] and page 10, paragraph [0088]. The choice of the reservoir layer can be the same or different as the primer layer, however when the polymers are the same, bonding between the layers is greater and creates a single-layered coating (i.e., a coating layer wherein the original coating is free of therapeutics). See page 5, paragraph [0053]. Hossainy also teaches a method of applying the composition to a stent then heating to evaporate the solvent. See page 2, paragraph [0016].

The instant invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made given the teachings of Hunter in view of Hossainy. Hunter teaches methods for the preparation of drug-loaded microspheres, which are provided as a coating onto a stent, whereby the drug (i.e., paclitaxel) is dissolved in a polymer solution containing a polymer and solvent (DCM), and wherein the solvent is evaporated to yield microspheres. Hunter teaches that the compositions can be in suitable forms, such as, for example, a paste, as in the form of a suspension wherein the microspheres are suspended in a hydrophilic gel, and thereafter the gel or paste can be smeared over tissue. Hunter also teaches compositions in the form of a film, whereby polymer is dissolved in a solvent, the solvent then evaporates and the polymer solidifies to form a film that can subsequently be peeled. The methods of Hunter are useful and effective for the treatment of angiogenic-dependent diseases and thus would include restenosis, as is instantly claimed. Hossainy teaches the use of a primer layer which allows for better adhesion of a therapeutic agent to the device. This allows for the use of multiple types of active agents as well as the option for multiple polymers in the composition. The main polymer used by Hossainy was ethylene-vinyl alcohol copolymer, which is different from the ethylene vinyl acetate of Hunter. However, the copolymers are very similar

in that both contain an ethylene monomer, as well as an ethylenically unsaturated monomer. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hunter with that of Hossainy, in which the copolymer of a stent coating composition would easily be interchangeable between ethylene vinyl acetate and ethylene-vinyl alcohol.

Maintained Rejections

Claim Rejections - 35 USC § 103

7. Claims 25, 30-32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter *et al.* (hereinafter "Hunter") (U.S. Pat. No. 5,886,026).

Hunter ('026) teaches methods for treating angiogenic-dependent diseases and compositions comprising anti-angiogenic factors and polymeric carriers, stents which have been coated with such compositions and methods for utilizing these stents and compositions (see column 1, lines 15-20); (col.3, line 42 - col. 5, line 43). Methods for the preparation of drug-loaded microspheres, films and pastes are also disclosed (see Examples).

The anti-angiogenic compositions may be fashioned in the form of microspheres of any size ranging from 50 nm to 500 μm (col. 17, lines 31-44). The compositions may also be prepared in paste or gel forms or as films (col. 17, line 45 - col. 18, line 10); (col. 37, lines 33-45). The anti-angiogenic compositions may be administered in combination with pharmaceutically or physiologically acceptable carriers, excipients or diluents (col. 37, lines 46-59).

Suitable polymeric carriers taught include poly(D,L-lactic acid), poly(glycolic acid), polycaprolactone, gelatin, starch, cellulose and polysaccharides for example and blends thereof (col. 16, lines 36-61). The anti-angiogenic compositions comprise a variety of active compounds in addition to the anti-angiogenic factors and polymeric carriers. Suitable active compounds are disclosed at column 15, lines 16-40).

The stents may be coated with the anti-angiogenic compositions or anti-angiogenic factors in a variety of ways, such as: (a) by directly affixing to the stent an anti-angiogenic composition (e.g., by either spraying the stent with a polymer/drug film or by dipping the stent into a polymer/drug solution), (b) by coating the stent with a substance such as a hydrogel which will absorb the anti-angiogenic composition or anti-angiogenic factor; (c) by interweaving the anti-angiogenic composition coated thread (or the polymer itself formed into a thread) into the stent structure, (d) by inserting the stent into a sleeve or mesh which is comprised of or coated with an anti-angiogenic composition or (e) constructing the stent itself with an anti-angiogenic composition (col. 22, lines 45-66).

The Examples at columns 42 onwards demonstrate various methods for the preparation of the anti-angiogenic compositions. For instance, Example 3 at column 42 demonstrates methods for the encapsulation of suramin whereby a polymer mixture is combined with the active agent (suramin) and solvent or reagent - dichloromethane (DCM). The process yields microspheres, wherein the polymer (PVA) encapsulates the active agent – suramin. Similarly, Example 4 at columns 42-43 demonstrates a procedure for the encapsulation of paclitaxel.

Example 8 at columns 45-47 outlines the manufacture of microspheres. Example 9 at columns 47-48 presents a process for the manufacture of a stent coating, wherein a sufficient

quantity of polymer and DCM are added in a vial and mixed by hand in order to dissolve the polymer. An appropriate amount of paclitaxel is added to the solution and dissolved by hand shaking. The stent is coated using a horizontal spraying technique, whereby the polymer and drug are deposited on the stent.

Procedures for producing a film are discussed at columns 51-52. The films may be made by for example, casting and spraying. In the casting technique, polymer is either melted and poured into a shape or dissolved in DCM and poured into a shape. The polymer then either solidifies as it cools or solidifies as the solvent evaporates. In the spraying technique, the polymer is dissolved in solvent and sprayed onto glass, as the solvent evaporates the polymer solidifies on the glass. Repeated spraying enables a buildup of polymer into a film that can be peeled from the glass (col. 51, lines 55-63).

Also see Example 14 at columns 60-61, which demonstrates thermopastes made up of polymer (PCL containing MePEG) loaded with paclitaxel.

Procedures for producing a nanopaste are discussed at columns 52-53. The nanopaste is a suspension of microspheres suspended in a hydrophilic gel. The gel or paste can be smeared over tissue as a method of located drug-loaded microspheres close to the target tissue.

Example 11 at columns 53-57 demonstrate controlled delivery of paclitaxel from microspheres composed of a blend of biodegradable poly(D,L-lactic acid) (PLA) polymer and non-degradable ethylene-vinyl acetate (EVA) copolymer. The microspheres are prepared by a solvent evaporation method.

The instant invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made given the teachings of Hunter. Hunter teaches methods

for the preparation of drug-loaded microspheres, which are provided as a coating onto a stent, whereby the drug (i.e., paclitaxel) is dissolved in a polymer solution containing a polymer and solvent (DCM), and wherein the solvent is evaporated to yield microspheres. Hunter teaches that the compositions can be in suitable forms, such as, for example, a paste, as in the form of a suspension wherein the microspheres are suspended in a hydrophilic gel, and thereafter the gel or paste can be smeared over tissue. Hunter also discloses compositions in the form of a film, whereby polymer is dissolved in a solvent, the solvent then evaporates and the polymer solidifies to form a film that can subsequently be peeled. The methods of Hunter are useful and effective for the treatment of angiogenic-dependent diseases and thus would include restenosis, as is instantly claimed.

Response to Arguments

Applicant's arguments filed March 15, 2010 have been fully considered but they are not persuasive.

Rejection under 35 U.S.C. 103(a) over Hunter et al.

8. Applicant argued, "the Examiner's comment that the prior art's method of preparation yields an end result essentially the same as that desired in the instant invention is irrelevant since the claims are directed to methods as opposed to product. Also, Applicant is unable to identify where Hunter discloses a stent coating of microparticles, because example 8 discusses the formation of microparticles, however example 9 forms a coating composition by a different method and it can not be assumed microparticles are formed. Applicant also argues that the Examiner has not established a *prima facie* case of obviousness and is using hindsight

knowledge to conclude the Applicant's claims are obvious. Regarding the use of microparticles in stent coatings, Hunter teaches away from this."

In response to Applicant's argument that the claims are to methods as opposed to products, it is agreed that the preamble is directed towards a method, however the intent of the comment is to prove that there is a reasonable expectation and predictable outcome when changing a coating method and achieving the same product.

In response to Applicant's argument that the claims do not identify a microparticle stent coating referencing the differences between examples 8 and 9 was not found persuasive because of the following reasons: the claims never state that the polymer should be a microparticle. Instead claim 25, and all of its dependents, state polymeric particles are used in the coating. With this said, example 9 is titled manufacture of stent coating wherein the coating is paclitaxel loaded polymers. Figures 48 and 49 both show particle diameter of the composition in microns. So even though example 9 does not necessarily discuss microparticles in the same manner as example 8, the use of microparticles in a stent coating is still taught as evidenced by Figures 48 and 49. Further evidence that the polymer is in particulate form is mentioned in column 17, lines 31-44. Hunter teaches that anti-angiogenic compositions can be fashioned in any size ranging from 50 nm to 500 μm, depending upon their particular use. For example "sprays", which solidify into a film or coating, are prepared from microspheres of a wide array of sizes. Therefore, it is maintained that Hunter teaches a stent coating comprising microparticles.

In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so

long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to Applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the Examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, the art is replete with traditional coating methods, including methods of coating a stent. It is obvious to one of ordinary skill in the art to apply a coating to stent, and then allow the coating to dry (i.e., solvent evaporation). Hunter teaches both spray drying and dipping wherein the coating is applied numerous times to achieve the desired coating thickness, with time between applications to allow the coating to dry (i.e., solvents to evaporate). See column 48, lines 10-59. Since Hunter also describe a similar coating composition as instantly claimed (polymeric particles and therapeutic agent), as well as spray drying and/or dipping techniques, it would have been obvious to one of ordinary skill in the art to coat a stent as instantly claimed.

In response to Applicant's fifth argument, it was not found persuasive that Hunter was teaching away from using microparticles in a stent coating because the microparticulate size

would prevent the therapeutic substance from being distributed uniformly. This is due to the fact that Hunter is actually stating what the coating should be able to do. Hunter teaches that the coating compositions should coat the stent smoothly and evenly. Hunter then teaches a coating composition comprising microparticles (based on Examples 8-10 and column 17, lines 31-44) of a therapeutic and polymer which is in the form of a suspension and is used to coat a stent. Hunter is silent as to whether this coating is uniform or not, however since this was the desired effect, and Hunter does not teach otherwise, it is assumed the coating was uniform. Therefore, Hunter does not teach away from coating stents with a microparticle composition but actually teaches that microparticulate material can effectively coat a stent.

For these reasons, the rejection on record has been maintained.

Correspondence

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JESSICA WORSHAM whose telephone number is 571-270-7434. The examiner can normally be reached on Monday - Thursday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JESSICA WORSHAM/
Examiner
Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner
Art Unit 1615

Application Number
10/663,181

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

EXAMINER'S CASE ACTION WORKSHEET

Copy (Ctrl+C)	Palm Transaction Code 1322 87639161510663181		Legal Instrument Examiner

CHECK TYPE OF ACTION DATE OF COUNT

☒ Non-Final Rejection	☐ Restriction/Election Only	☐ Final Rejection
☐ Ex Parte Quayle	☐ Allowance	☐ Advisory Action
☐ Examiner's Answer	☐ Reply Brief Noted	☐ Non-Entry of Reply Brief
☐ Defective Notice of Appeal	☐ Interference Disposal SPE ____ (Approval for Disposal)	☐ Suspension (Examiner-Initiated) SPE ____ (*initial*)
☐ Defective Appeal Brief	☐ SIR Disposal (use only after FAOM)	☐ Supplemental Examiner's Amendment
☐ Miscellaneous Office Letter (With Shortened Statutory Period Set)	☐ Notice of Non-Responsive Amendment (With One Month Time Period set)	☐ Miscellaneous Office Letter (No Response Period Set)
☐ Abandonment after BPAI Decision	☐ Supplemental Action	☐ Response to Rule 312 Amendment
☐ Letter Restarting Period for Response (e.g., Missing References)	☐ Interview Summary	☐ Authorization to Change Previous Office Action SPE: ____ (*Initial*)
☐ Abandonment	☐ Express Abandonment Date: ____	☐ Other

Examiner's Name: JESSICA WORSHAM **AU:** 1615